Remarks

Claims 1-7 are pending.

As a preliminary matter, Applicant notes that an initialed Form PTO-1449 listing the references submitted with the Supplemental Information Disclosure Statement dated August 6, 2003, was not returned with the final Office Action. Applicant again requests the Examiner to confirm consideration of the references cited in the Supplemental IDS.

In the final Office Action, the Examiner maintained the rejections of claims 1-7 under 35 U.S.C. § 101 as lacking utility and under 35 U.S.C. § 112, first paragraph, as lacking an enabling description of how to use the claimed invention. Both rejections are grounded on the supposed lack of utility for the claimed knockout mice, which are resistant to the amnesic effects of scopolamine. These rejections are again traversed based on the following reasons, which supplement those set forth in the remarks provided with the Amendment filed February 24, 2004, which are incorporated by reference herein.

In addressing Applicant's previous arguments, the Examiner argued that "[f]urther research does not have a specific or substantial utility." The Examiner's reasoning would appear to, in effect, knock out the patentability of knockout animals and other research tools *per se*, even though research tools have been recognized as having value in the industry (see Integra LifeSciences I Ltd. v. Merck KGaA, 66 U.S.P.Q.2d 1865 (Fed. Cir. 2003)). The fact that a research tool has a real-world value reflects that it has a practical and substantial utility. Thus, the fact that Toyota has made practical use of such transgenic mice to research receptor roles provides

evidence supporting, rather than negating, that the claimed mice's utility is indeed substantial.

Furthermore, that the claimed H3-/- mice have substantial utility flows from the already identified utilities of the histamine H3 receptor. The Examiner's arguments overlook the fact that the histamine H3 receptor is not an orphan receptor. Although the instant specification, like the literature, reflects that *all* of the functions or roles of the receptor in signaling pathways or biological mechanisms have yet to be fully elucidated or validated, the instant specification and prior art nonetheless describe some functions or roles of the receptor that are credible. See, e.g., WO 95/11894 and Perez-Garcia et al. (Psychopharmacology, 1999, 142:215-220), both of which are cited in the Supplemental IDS. For example, WO 95/11894 notes that histamine H3 receptor antagonists have utility in treating dementia disorders, such as Alzheimer's disease. Indeed, as indicated at page 10 of the present specification, the phenotypic findings correlate with the role of the receptor in cholinergic pathways modulating memory function or cognitive processes. Thus, modulators of histamine H3 receptor activity have substantial and credible utility, and likewise the claimed H3-/- mice have substantial and credible utility as a pharmaceutical research and development tool, e.g., to help screen or develop such histamine H3-modulating compounds.

As evident from the foregoing, a person of ordinary skill in the art would readily appreciate that the invention has a utility that is specific, substantial, and credible. Moreover, the making and use of the invention is supported by an enabling disclosure.

The Examiner, in arguing that the full scope of the claimed invention is not enabled, asserted that the "claims encompass any disruption of any histamine H3 receptor gene." To the contrary, the claims specify that the disruption is generated by targeted replacement with a non-functional histamine H3 receptor gene and results in the mouse having an insensitivity to amnesic effects of scopolamine as demonstrable in a passive avoidance test as compared to wild-type histamine H3 receptor mice. See also page 9, lines 10-15, of the instant specification, regarding the verification of total absence of H3 receptors in the exemplified transgenic mice. The Examiner has failed to explain why, considering the examples, teachings and other guidance provided in the present disclosure, coupled with the knowledge in the art, it would take more than routine experimentation to identify viable disruptions and therefore to make and use mice within the scope of the claims. Consequently, a *prima facie* case of non-enablement has not been established.

As shown above, the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, are in error. Applicant therefore requests that these rejections be withdrawn.

Applicant also requests withdrawal of the rejection of claim 5 under 35 U.S.C. § 112, second paragraph. The Examiner maintained the rejection for indefiniteness, stating that the phrase "the blastocyst" in step (c) of claim 5 lacks antecedent basis. Applicant notes, however, that the recited terminology in step (c) is "the blastocysts", which unambiguously is in reference to the antecedent "blastocysts" first recited in step (a).

In view of the foregoing, the application is in condition for allowance. Applicant therefore requests prompt and favorable action.

Respectfully submitted,

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